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A Comparative Study of Platelet Indices, in Cases of Fever, Sepsis Leading To Multiorgan Dysfunction And Control Group, At A Tertiary Care Hospital Using An Automated Hematology Analyzer Sysmex Xn_1000

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Abstract
Introduction: *Platelet indices are a group of derived platelet parameters obtained as a part of the automatic complete blood count.Emerging evidence suggests that Platelet indices may have diagnostic and prognostic value in certain diseases.Hence, simultaneous measurement of all platelet indices (MPV, PDW, P-LCR, PCT and PC) will provide a valid instrument for measuring disease.*
Aims & Objectives*: To compare the parameters of platelet indices (MPV, PDW, P-LCR, PCT and PC) A] in patients with fever and B] in patients with sepsis leading to multiorgan dysfunction ,with control cases.*
Materials & Methods: *Platelet indices of 100 consecutive hemograms with a clinical diagnosis of fever, 100 consecutive hemograms with a clinical diagnosis of MODS (Sepsis with Multiorgan dysfunction) were retrieved. The analysis was done on a Sysmex XN-1000 automated blood cell counter. The parameters of PIs were analyzed statistically using IBM SPSS version 22.*
Results:*The difference in mean PDW between controls and MODS was statistically significant (p value=0.004). The difference in mean MPV between controls and MODS was statistically significant (p value=0.021). The difference in mean PLCR between controls and MODS was statistically significant (p value=0.005). The difference in mean PCT between controls and Fever was statistically significant (p value<0.001).The difference in mean PC between None of the groups was statistically not significant.*
Conclusions: *Among the parameters P-LCR has shown highest predictive validity, followed by MPV and PDW.Considering all the AUC values very close to the null value of 0.5, none of the indices analysed were strong predictors of MODS. A prospective study with a larger sample size and follow up, may help in deriving a predictive value.*

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I. Introduction

Platelets are dynamic blood particles whose primary function, along with coagulation factors is hemostasis and there is accumulating evidence that platelets contribute to the inflammatory process, microbial host defense, wound healing, angiogenesis and remodeling. (1)

Platelets also mediate leukocyte movement from the blood stream through the vessel wall to tissues and are capable of forming reactive oxygen species and the oxidative stress that accompanies inflammation can also activate platelets.(2,3)Platelets ability to influence other cells indicates that they can also play many principle roles in the pathophysiology of diseases.Platelet indices are a group of derives platelet parameters obtained as a part of the automatic complete blood count.Emerging evidence suggests that Platelet indices may have diagnostic and prognostic value in certain diseases.Hence, simultaneous measurement of all platelet indices(MPV,PDW, P-LCR, PCT and PC) will provide a valid instrument for measuring disease.

Platelet parameters are obtained as a part of the automatic complete count, without any extra cost.

II. Aims & Objectives:

1. To compare the parameters of platelet indices (MPV,PDW,P-LCR, PCT and PC)in patients with fever and B] in patients with sepsis leading to multiorgan dysfunction with control cases.
2. To determine the significance of platelet indices in assessing the severity of inflammation.
3. To determine the role of PIs as a prognostic/diagnostic marker, either individually or in combination.
4. To compare the results, with other similar studies.

III. Materials and Methods

The present study is a retrospective study, done at a tertiary care hospital, in south India.

3.1Inclusion criteria

1. Platelet indices of 100 consecutive hemograms with a clinical diagnosis of fever, 100 consecutive hemograms with a clinical diagnosis of MODS(Sepsis with Multiorgan dysfunction) were retrieved.
2. The analysis was done on a Sysmex XN-1000 automated blood cell counter.
3. 100 consecutive hemograms, marked as negative, in counter analysis, were taken as controls.
4. The data was retrieved over a period of 1year (July 2016-July 2017).

3.2Exclusion criteria

1. Cases with diagnosis of fever and MODS, which showed error on analysis with automated blood cell counter, were excluded.
2. The parameters of PIs were analyzed statistically.

IV. Statistical methods

Various platelet indices (MPV, PDW, P-LCR, PCT & PC) were considered as primary outcome variables. Study group (Controls, fever and presence of MODS) were considered as primary explanatory variables.

V. Descriptive Analysis

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Data represented using box plots.

1. The association between explanatory (i.e. controls, Fever and MODS) and outcome variables (MPV, PDW, P-LCR, PCT & PC) was assessed by comparing the mean values.
2. One-way ANOVA was used to assess statistical significance.
3. The ability of various Platelet indices in predicting MODS was assessed by Receiver Operating curve (ROC) analysis. The area under curve (AUC) and it's 95% CI and P-value were presented.
4. P value < 0.05 was considered statistically significant.
5. IBM SPSS version 22 was used for statistical analysis.[4]
6.

VI. Results

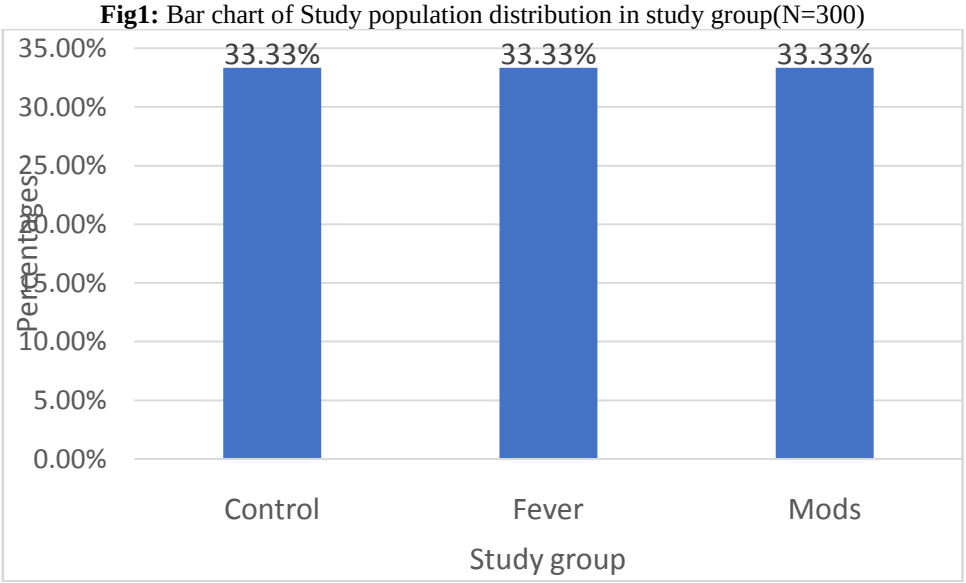
A total of 300 subjects were included in the analysis.

Among the study population, the study group was control in 100(33.33%), Fever in 100(33.33%) and MODS in 100(33.33%). (Table 1)

Table1: Descriptive analysis of Study population in study group (N=300)

Study group	Frequency	Percentages
Control	100	33.33%
Fever	100	33.33%
Sepsis with MODS	100	33.33%

Fig1: Bar chart of Study population distribution in study group(N=300)



VII. Inferential Analysis

Table2: Comparison of mean of platelet indices across study groups (N=300)

Parameter	Control (Mean ± Std. Dev)	Fever (Mean ± Std. Dev)	MODS (Mean ± Std. Dev)	P value (Control Vs Fever)	P value (Control Vs MODS)
PDW	11.81±1.938	12.50±3.056	12.99±3.347	0.084	*0.004*
MPV	10.42±0.913	10.48±1.448	11.00±2.554	0.802	*0.021*
PLCR	27.95±7.309	26.31 ±12.57	31.95 ±9.137	0.242	*0.005*
PCT	0.287 ± 0.083	3.025 ± 8.493	0.392 ± 1.104	*<0.001*	0.880
PC	2.914 ± 1.537	2.585 ± 1.765	2.823 ± 2.196	0.210	0.729

1. The mean PDW in control group was 11.81±1.938, among fever cases was 12.50±3.056 and in people with MODS was 12.99±3.347. The difference in mean PDW between controls and MODS was statistically significant (p value=0.004).
2. The mean MPV in control group was 10.42±0.913, among fever cases was 10.48±1.448and in people with MODS was 11.00±2.554. The difference in mean MPV between controls and MODS was statistically significant (p value=0.021).
3. The mean PLCR in control group was 27.95±7.309, among fever cases was 26.31 ±12.57 and in people with MODS was 31.95 ±9.137. The difference in mean PLCR between controls and MODS was statistically significant (p value=0.005).
4. The mean PCT in control group was 0.287 ± 0.083, among fever cases was 3.025 ± 8.493and in people with MODS was 0.392 ± 1.104. The difference in mean PCT between controls and Fever was statistically significant (p value<0.001).
5. The mean PC in control group was 2.914 ± 1.537, among fever cases was 2.585 ± 1.765and in people with MODS was 2.823 ± 2.196. The difference in mean PC between None of the groups was statistically not significant.

Fig 2: Comparisons of PDW Across the study group(N=300)

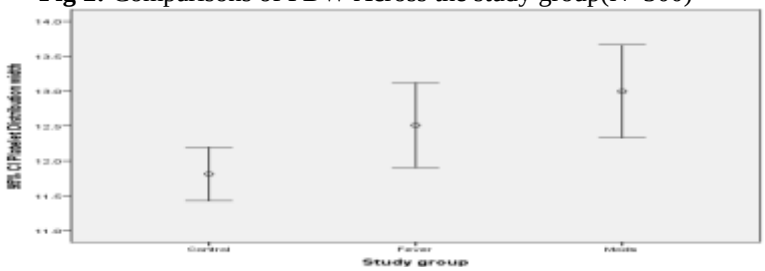


Fig3: Comparisons of MPV Across the study group(N=300)

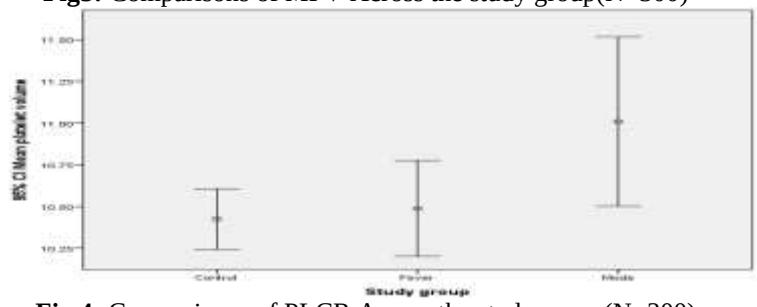


Fig 4: Comparisons of PLCR Across the study group(N=300)

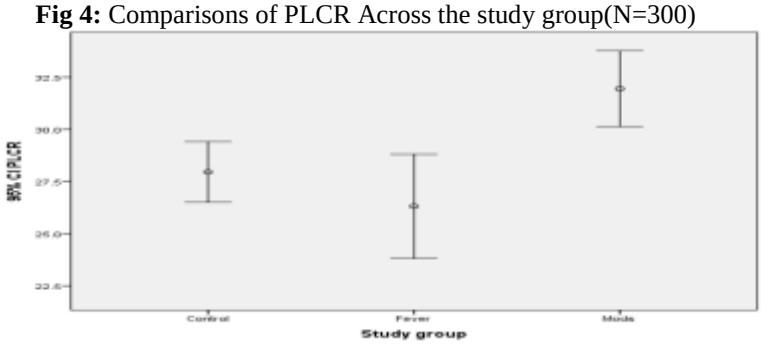


Fig 5: Comparisons of PCT Across the study group(N=300)

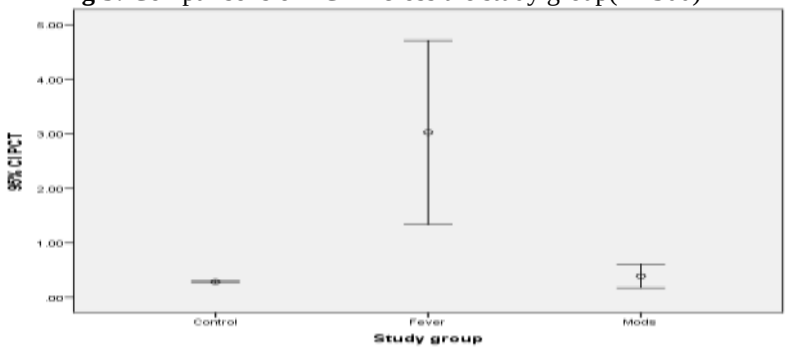


Fig 6: Comparisons of PC Across the study group(N=300)

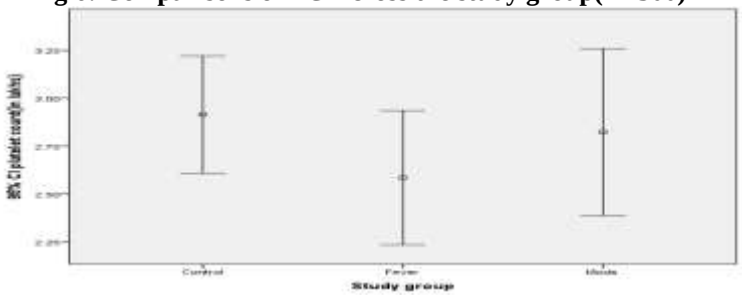
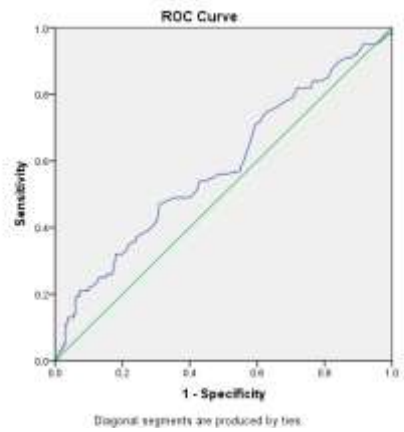


Table 3: Predictive validity of Different indices in predicting MODS(N=300)

Parameter	Area under the curve	95% CI		P value
		Lower	Upper	
PDW	0.581	0.512	0.651	0.021
MPV	0.607	0.539	0.676	0.002
PLCR	0.625	0.558	0.691	<0.001
PCT	0.467	0.395	0.540	0.354
PC	0.477	0.403	0.550	0.507

The area under the curve for PDW in predicting MODS was 0.581 (95% CI 0.512 to 0.651), which was statistically significant (P value 0.021). The area under the curve for MPV in predicting MODS was 0.607 (95% CI 0.539to 0.676), which was statistically significant (P value 0.002). The area under the curve for PLCR in predicting MODS was 0.625 (95% CI 0.558 to 0.691), which was statistically significant (P value< 0.001). The area under the curve for PCT in predicting MODS was 0.467 (95% CI 0.395 to 0.540), which was statistically not significant (P value= 0.354). The area under the curve for PC in predicting MODS was 0.477 (95% CI 0.403 to 0.550), which was statistically not significant (P value=0.507).

Fig 7: **Predictive validity of Platelet Distribution Width (PDW)in predicting MODS**



AUC:0.581

P value:0.021

Fig 8: Predictive validity of Mean platelet volume(MPV)in predicting MODS

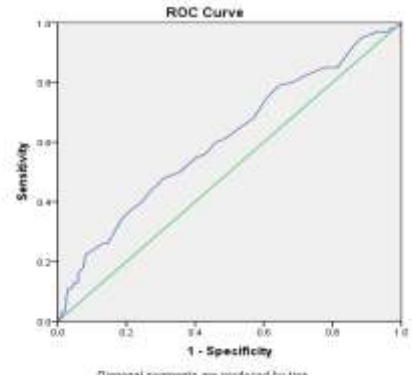


Fig 9: Predictive validity of PLCR in predicting MODS

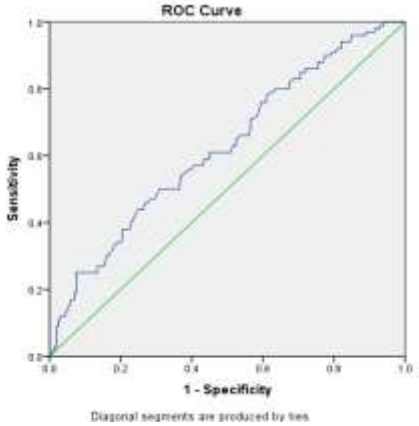


Fig 510predictive validity of PCTin predicting MODS

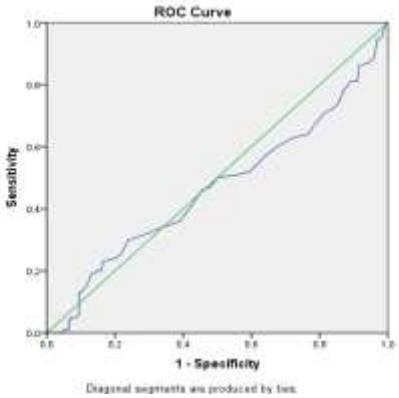
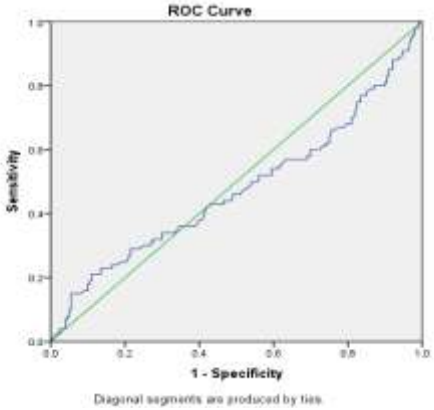


Fig 11: Predictive validity of platelet count (in lakhs) in predicting MODS



VIII. Discussion

The present study is a retrospective study, done at a tertiary care hospital, in south India. The various platelet indices (MPV,PDW,P-LCR, PCT and PC) considered as outcome variables were compared among controls , cases with clinical diagnosis of fever and cases with clinical diagnosis of MODS(Sepsis with multiorgan dysfunction), which were considered as explanatory variables.

The platelet indices in 100 consecutive cases marked as negative in the output of the cell counter (Sysmex XN-1000) were taken as controls. 100 consecutive cases with clinical diagnosis of fever and 100 consecutive cases with clinical diagnosis of MODS were analysed, using IBM SPSS version 22.In the present study, the mean values of various platelet indices(PDW, MPV and P-LCR) are increasing when compared between, controls, cases with fever and cases with clinical diagnosis of Multiorgan dysfunction due to sepsis.Also , the difference in mean PLCR between controls and MODS was statistically significant (p value=0.005), Hence, a rise in PLCR indicates, severity of inflammation and therefore, poor prognosis . These findings correlated with other studies in the literature.In a retrospective study of 124 patients with septic shock, divided into survivor and non-survivor groups,Yanxia Gao et al 2014[(12)] observed that MPV,P-LCR and PDW were increasing, while PLT and PCT were decreasing with time. In an another study Pattrapom T et al 2016[(10)] ,a retrospective study, the rise in MPV and to a lesser extent an increase in P-LCR and PDW, was indicative of a worse prognosis in patients with septic shock. A statistical difference in MPV was seen between the non survivors and the survivors of the septic shock.In the present study, the difference in mean PDW between controls and MODS was statistically significant (p value=0.004). This finding correlated with a study by Akasu S et al 2005 [(16)] ,where PDW was more elevated in non-survivors. In the present study, the difference in mean MPV between controls and MODS was statistically significant (p value=0.021). The difference in mean PCT between controls and Fever was statistically significant (p value<0.001).The difference in mean PC between None of the groups was statistically not significant.These findings also correlated with other studies in the literature.

Vanderlelie et al 1983 [(14)] showed that MPV was elevated in 13 of the 25 septicemia patients and returned to normal values as soon as the disease was under control.In 2 different new born cohorts with sepsis by Guida eat al 2003 [(15)], thrombocytopenia and high MPV appeared to be prominent. MPV was not increased in local infection or sepsis with negative blood culture. They suggested , an elevated MPV indicates that the infection is invasive, systemic and uncontrolled an is releated to the severity of the disease and therefore MPV may be a useful assessment tool for prognostic features of septic shock.Chen Hokim et al 2015 [(17)] revealed a greater increase of MPV in non-survivors of severe sepsis and or septic shock compared with survivors during the first 72hrs after hospitalization and found that an increase in MPV from baseline is an independent risk factor of mortality.In the present study the area under curve AUC for P-LCR was higher (0.62), followed by MPV(0.60) and PDW(0.58).In a study from India, Babu E et al (2004) [(18)] compared the 5 major platelet indices. The MPV had the highest precision rate of 75.6% and higher AUC(0.81) followed by P-LCR(0.76) and PDW(0.75). But the AUC of PDW and P-LCR are lower than the MPV.In the present study,the area under the curve for PDW in predicting MODS was statistically significant (P value 0.021). The area under the curve for MPV in predicting MODS was statistically significant (P value 0.002). The area under the curve for PLCR in predicting MODS was statistically significant (P value< 0.001). The area under the curve for PCT and PC in predicting MODS was statistically not significant (P value=0.507).Yanxia Gao et al 2014 [(12)] observed that MPV over 10.5 on admission and on the first 3 days after admission was a good predictor of mortality in patients with septic shock.

In the present study, a definitive predictive value for various platelet indices could not be derived, as the AUC was close to null value (0.5).

IX. Conclusion

1. Among the parameters P-LCR has shown highest predictive validity, followed by MPV and PDW.
2. P- LCR , is often correlated to MPV but is more sensitive to changes in platelet size.
3. But considering all the AUC values very close to the null value of 0.5, none of the indices analysed were strong predictors of MODS.
4. This is probably because the present study is a retrospective study, based on the clinical diagnosis, where follow up values were not interpreted. Hence, a prospective study with a larger sample size and follow up, may help in deriving a predictive value.
5. Newer platelet parameters, Immature platelet fraction(IPF), Mean platelet component(MPC), Platelet component distribution width (PCDW) and Mean platelet mass (MPM),to determine the changes in the status of platelet activation would be of much help in assessing the severity of inflammation, in near future.

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